The Office Action states that Information Disclosure Statement filed March 26, 1997 fails to comply with the provisions of M.P.E.P. § 609 because an improper form PTO-1449 or equivalent was submitted. Specifically, the Action states that each of the EMBL database submissions listed on the IDS fails to recite the name of the author and the date of publication. The Action also notes that the names of the authors and the dates of publication for these EMBL database submissions have been added to the form PTO-1449, with the corrected document being made of record.

Applicants presume that the Information Disclosure Statement of which the Action refers is the Information Disclosure Statement filed June 20, 2001. Applicants thank the Examiner for correcting the form PTO-1449 by adding the authors' names and publication dates for the EMBL database submissions listed on the IDS. Applicants believe that the corrected form PTO-1449 complies with the provisions of M.P.E.P. § 609, and note that the Action states that the corrected PTO-1449 has been made of record. However, Applicants would be happy to supply an updated copy of the Information Disclosure Statement, and would prefer to have the opportunity if the deficiencies in their previously-submitted Information Disclosure Statement will have the effect of leaving any of the cited references off the front page of any issued patent.

3. Objection to the specification

The Office Action contains an objection to the specification because there are blank spaces in place of an ATCC deposit number on pages 3-5, 9, and 97. Applicants have amended the specification to delete reference to an ATCC deposit number in the specification, and therefore, respectfully request that the objection be withdrawn.

4. Rejections of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 101

The Office Action asserts a rejection of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 101. The Action states that the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. Applicants traverse this rejection.

Applicants contend that the instant application contains an assertion of a specific and substantial utility for the claimed invention that would be credible to one of ordinary skill in the art. The Source and the first of the court of the property and think an amino of the common factor that I

Accession No. AAH13644 (replication initiation region protein), which shares the lowest degree of sequence identity with IL-1ra-L polypeptide, *all* of the related amino acid sequences identified in a BLAST search using the IL-1ra-L amino acid sequence (SEQ ID NO: 2) are members of the IL-1 family of proteins (Exhibit A; sequences that were publicly available at the time the instant application was filed are indicated in bold). Based on the knowledge in the art at the time the instant application was filed, Applicants contend that one of ordinary skill in the art would recognize that IL-1ra-L polypeptide is a member of the IL-1 family of proteins. Moreover, as members of the IL-1 family have substantial real world use, for example, as agonists or antagonists of inflammatory responses via binding to an interleukin receptor (Gabay, 2000, *Expert Opin. Investig. Drugs* 9:113-27), Applicants contend that one or ordinary skill in the art would recognize that the claimed molecules have credible, specific, and substantial utility.

Applicants contend that because the instant application contains an assertion of a specific and substantial utility for the claimed invention credible to one of ordinary skill in the art, the rejection under 35 U.S.C. § 101 should be withdrawn.

5. Rejections of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 112, first paragraph

The Office Action asserts a rejection of claims 1-8, 10, 11, and 42-46, under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention. The Action states that since the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility, one skilled in the art would not know how to use the claimed invention.

Applicants have set forth affirmative evidence that the asserted utility would be credible to one of ordinary skill in the art. Applicants contend that because the instant application contains an assertion of a specific and substantial utility for the claimed invention that one of ordinary skill in the art would find to be credible, this rejection should be withdrawn.

The Office Action also asserts a rejection of claims 1, 2, 4-8, 10, 11, and 42-46, under 35 U.S.C. § 112, first paragraph, as containing subject matter that was not described in the specification.

necessary for the enablement of the claims because the specification does not provide a repeatable method for obtaining "ATCC Deposit No. ______" and this deposit does not appear to be a readily available material. The Action also states that a deposit made in full compliance with 37 C.F.R. §§ 1.803-1.809 would satisfy the requirements of 35 U.S.C. § 112, first paragraph, provided that Applicants submit an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that a deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent.

Applicants have amended claim 1 so that it no longer recites a nucleic acid molecule comprising the nucleotide sequence of the DNA insert in "ATCC Deposit No. ..." In addition. Applicants have amended claim 2 so that it no longer recites nucleic acid molecules comprising a region of the DNA insert in "ATCC Deposit No. ." encoding a polypeptide fragment of at least 25 amino acid residues, or a region of the DNA insert in "ATCC Deposit No. ," comprising a fragment of at least 16 nucleotides. Applicants respectfully contend that because claims 1 and 2, as amended, delete reference to an ATCC deposit number, this ground of rejection is moot.

The Office Action also asserts a rejection of claims 2, 3-8, 10, 11, and 42-46, under 35 U.S.C. § 112. first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The Action states that because the genus of IL-1ra-L variants recited in claims 2 and 3 is highly variant, and the specification fails to describe the common attributes or characteristics identifying the members of this genus, or provide a representative number of species to describe this genus, the Applicants were not in possession of the claimed genus of nucleic acid molecules at the time the application was filed.

Applicants have amended claim 2 to recite an isolated nucleic acid molecule comprising a region of the nucleotide sequence of SEQ ID NO: 1 encoding a polypeptide fragment of at least 25 amino acid residues; a region of the nucleotide sequence of SEQ ID NO: I comprising a fragment of Control of the state of the factories and the state of th

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a nucleotide sequence complementary to the nucleotide sequence of any of the above nucleic acid molecules. Applicants contend that because claim 2, as amended, recites only fragments of the disclosed human IL-1ra-L nucleic acid molecule (*i.e.*, SEQ ID NO: 1), one of ordinary skill in the art could readily determine the structure of nucleic acid molecules falling within the scope of this claim. Applicants therefore respectfully request that this ground of rejection be withdrawn.

Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 2; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 having a C- and/or N- terminal truncation, wherein the encoded polypeptide comprises at least 25 amino acid residues; a region of the nucleotide sequence of any of these nucleic acid molecules comprising a fragment of at least 16 nucleotides, a nucleotide sequence that hybridizes under at least moderately stringent conditions to the complement of the nucleotide sequence of any of the above nucleic acid molecules; or a nucleotide sequence complementary to any of the above nucleic acid molecules. Applicants note that the instant application teaches the amino acid sequence for human IL-1ra-L polypeptide (Figures 1A-1B). The instant application further sets forth in Table I (pages 21-22) rubrics recognized in the art for making conservative amino acid substitutions. In view of the teachings in the instant application. Applicants respectfully contend that one of ordinary skill in the art would understand the scope of species comprising the disclosed genus, and that the inventors were in possession of the invention having said scope at the time the application was filed. Thus, Applicants respectfully contend that their specification fulfills the requirements of 35 U.S.C. § 112, first paragraph, and request that this ground of rejection be withdrawn.

The Office Action also asserts a rejection of claims 2-8, 10, 11, and 42-46, under 35 U.S.C. § 112. first paragraph, because the specification while being enabling for a nucleic acid encoding a polypeptide as set forth in SEQ ID NO: 2, does not reasonably provide enablement for a nucleic acid encoding a polypeptide which is "at least about 70% identical to the polypeptide of SEQ ID NO: 2" or a nucleic acid molecule encoding a substitution, insertion, or deletion mutant of the polypeptide of SEQ ID NO: 2. The Action states that because the claims are overly broad, no guidance is provided

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in the art that even a single amino acid change in the amino acid sequence of a protein can have a dramatic effect on that protein's function, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

As described above, Applicants have amended claims 2 and 3 so that they no longer recite nucleic acid molecules comprising either a nucleotide sequence encoding a polypeptide which is at least about 70 percent identical to the polypeptide as set forth in any of SEQ ID NO: 2; a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide sequence as set forth in any of SEQ ID NO: 1; a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid insertion, or a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid deletion. Applicants contend that the claims, as amended, are not overly broad, and that in view of the specification's teachings, one of ordinary skill in the art could readily make and use the claimed nucleic acid molecules. Moreover, Applicants contend that while the references cited in the Action may teach that an amino acid change in the amino acid sequence of a protein can have a dramatic effect on that protein's function, these references do not teach that a *conservative* amino acid substitution would have this effect. Specifically, Mikayama et al., 1993, Proc. Natl. Acad. Sci. U.S.A. 90:10056-60, teach that an asparagine-to-serine substitution at position 106 in human GIF destroys GIF function, and Voet et al., Biochemistry 126-28, 228-34 (1990), teach that a glutamic acid-to-valine substitution in beta hemoglobin results in sickle-cell anemia. These are *not* "conservative substitutions" as that term is understood by those with skill in the art or as explicitly defined in the instant specification. Applicants note that the instant specification does not teach that an asparagines-to-serine substitution or a glutamic acid-to-valine substitution is either exemplary or preferred (Table I; pages 22-22). Applicants contend that, in view of the specification's teachings and knowledge in the art, it would not require undue experimentation for one of ordinary skill in the art to make and use the claimed invention, and therefore, Applicants respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, first paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

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Rejections of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 112, second paragraph 6.

The Office Action asserts a rejection of claims 1-8, 10, 11, and 42-46, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as their invention.

The Action first asserts that claims 1-3 are indefinite for reciting the phrase "hybridizes under moderately or highly stringent conditions" because this phrase is relative and conditional. The Action states that some nucleic acids that might hybridize under conditions of moderate stringency would fail to hybridize under conditions of high stringency. Applicants note that the specification defines the meaning of the terms "moderately stringent conditions" (page 18, lines 1-7) and "highly stringent conditions" (page 16, line 26 to page 17, line 2), and provides examples of each. However, in order to more particularly point out and distinctly claim the subject matter that Applicants regard as their invention, Applicants have amended claims 1-3 to recite that the claimed nucleic acid molecules comprise a nucleotide sequence that "hybridizes under at least moderately stringent conditions." Applicants contend that the claims, as amended, are not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claim 2 is vague for reciting the phrase "about 70% identical" because the term "about" is inherently vague and indefinite. As discussed in section 5 above, Applicants have amended claim 2 so that it no longer recites a nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide which is at least about 70 percent identical to the polypeptide as set forth in any of SEQ ID NO: 2. In addition, Applicants have amended claim 2 to replace the term "at least about 25 amino acid residues" with the term "at least 25 amino acid residues," and claims 2 and 3 to replace the term "at least about 16 nucleotides" with the term "at least 16 nucleotides." Applicants contend that the claims, as amended, are not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claims 2 and 3 are vague and indefinite for reciting the phrase "has an activity of the polypeptide set forth in ... SEQ ID NO: 2" because the activity of the polypeptide encoded by the nucleic acid being claimed is unclear. While Applicants respectfully disagree with the assertion that this phrase is indefinite, in an effort to expedite the present application

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must comprise at least 25 amino acid residues. Applicants contend that the claims, as amended, are not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claim 10 is vague and indefinite for reciting the phrase "other than the promoter DNA for the native IL-1ra-L polypeptide" because it is unclear which promoter DNA is being excluded and which is being included in the claim. Applicants have amended claim 10 to recite that "the nucleic acid molecule comprises promoter DNA other than native IL-1ra-L promoter DNA." Applicants contend that because it is clear which promoter DNA is being excluded and which is being included, claim 10 is not indefinite, and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claim 46 is indefinite for reciting the term "fragment[s] thereof" because this term encompasses potentially any portion of the heterologous polypeptide including a single amino acid. Applicants have amended claim 46 to recite that the IgG constant domain fragment must be "biologically-active," and therefore, respectfully request that this ground of rejection be withdrawn.

The Action next asserts that claims 45 and 46, which are dependent upon non-elected claims 13. 14, or 15, should be amended to be dependent upon on elected nucleic acid claims, since the nucleic acid is utilized in production of the fusion proteins. Applicants have amended claims 45 and 46 to recite a nucleic acid molecule encoding a fusion polypeptide comprising the nucleic acid molecule of any of claims 1, 2, or 3 fused to DNA encoding a heterologous amino acid sequence. Because claims 45 and 46, as amended, are no longer dependent upon non-elected claims 13, 14, or 15. Applicants request that this ground of rejection be withdrawn.

The Action next asserts that claims 4-8, 11, and 42-44 are vague and indefinite for being dependent upon claims 1 and 2 for their limitations. Applicants contend that the claims, as amended. satisfy the requirements of 35 U.S.C. § 112, second paragraph, and therefore, respectfully contend that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 112, second paragraph, have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

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7. Rejections of claims 1-8, 10, 11, and 42-46 under 35 U.S.C. § 102

The Office Action asserts a rejection of claims 1-8, 10, 11, and 42-46, under 35 U.S.C. § 102(a), as being anticipated by International Publication No. WO 99 37662 (published July 29, 1999), contending that this reference discloses a nucleotide sequence of a cDNA molecule encoding a SPOIL protein, which would be capable of hybridizing under moderately stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 1, or which, in the absence of an upper limit to the number of substitutions, deletions, or insertions, would meet the limitations of claim 3. Applicants traverse this rejection.

Applicants first note that the cDNA molecule disclosed in International Publication No. WO 99/37662 shares a sequence identity of 30.2% with the nucleotide sequence of SEQ ID NO: 1 (Exhibit B). In view of the specification's teaching that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79% (page 18. lines 6-7), it is quite apparent that the cDNA molecule disclosed in WO 99/37662 would *not* hybridize to the nucleotide sequence of SEQ ID NO: 1 under Applicants' recited stringency conditions. In addition, as described in section 6 above. Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 2. Applicants contend that claim 3, as amended, does not encompass the cDNA molecule disclosed in WO 99/37662. Applicants contend. therefore, that International Publication No. WO 99/37662 cannot anticipate the claims of the instant application, and respectfully request that this ground of rejection be withdrawn.

The Office Action next asserts a rejection of claims 1-8, 10, 11, and 42-46, under 35 U.S.C. § 102(b), as being anticipated by European Patent Application No. EP 0.855,404 (published July 29, 1998), contending that this reference discloses a nucleotide sequence of a cDNA molecule encoding an II.-Tra beta protein, which would be capable of hybridizing under moderately stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 1, or which, in the absence of an upper limit to the number of substitutions, deletions, or insertions, would meet the limitations of claim 3. Applicants traverse this rejection.

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(Exhibit C). As discussed above, in view of the specification's teaching that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79%, it is quite apparent that the cDNA molecule disclosed in EP 0.855 404 would *not* hybridize to the nucleotide sequence of SEQ ID NO: 1 under Applicants' recited stringency conditions. In addition, as described in section 6 above. Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide *is at least 70 percent identical* to the polypeptide set forth in SEQ ID NO: 2. Applicants contend that claim 3, as amended, does not encompass the cDNA molecule disclosed in EP 0.855 404. Applicants contend, therefore, that European Patent Application No. EP 0.855 404 cannot anticipate the claims of the instant application, and respectfully request that this ground of rejection be withdrawn.

The Office Action next asserts a rejection of claims 1-8, 10, and 42, under 35 U.S.C. § 102(b), as being anticipated by U.S. Patent No. 5,075,222 (issued December 24, 1991), contending that this reference discloses a nucleotide sequence of a cDNA molecule encoding an IL-1ra protein, which would be capable of hybridizing under moderately stringent conditions to the complement of the nucleotide sequence of SEQ ID NO: 1, or which, in the absence of an upper limit to the number of substitutions, deletions, or insertions, would meet the limitations of claim 3. Applicants traverse this rejection.

Applicants first note that the cDNA molecule disclosed in U.S. Patent No. 5.075,222 shares a sequence identity of 36.5% with the nucleotide sequence of SEQ ID NO: 1 (Exhibit D). As discussed above, in view of the specification's teaching that nucleic acid molecules capable of hybridizing under moderately stringent conditions will share a sequence identity of approximately 79%, it is quite apparent that the cDNA molecule disclosed in U.S. 5.075,222 would *not* hybridize to the nucleotide sequence of SEQ ID NO: 1 under Applicants' recited stringency conditions. In addition, as described in section 6 above. Applicants have amended claim 3 to recite an isolated nucleic acid molecule comprising a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one conservative amino acid substitution, wherein the encoded polypeptide *is at least 70 percent*

MicDonnell Boehnen Hulbert & Berghoff 300 South Warker Drive that U.S. Patent No. 5,075,222 cannot anticipate the claims of the instant application, and respectfully request that this ground of rejection be withdrawn.

Applicants respectfully contend that rejections based on 35 U.S.C. § 102 have been overcome by amendment or traversed by argument, and request that the Examiner withdraw all rejections made on this basis.

CONCLUSIONS

Applicants respectfully contend that all conditions of patentability are met in the pending claims as amended. Allowance of the claims is thereby respectfully solicited.

If Examiner Mertz believes it to be helpful, she is invited to contact the undersigned representative by telephone at (312) 913-0001.

Respectfully submitted,

McDonnell Boehnen Hulbert & Berghoff

Dated: January 16, 2003

By

Donald L. Zuhn, Ph.D

Reg. No. 48,710



EXHIBIT A

STP 2.2.5 [Nov-16-2002]

Reference:

Altschul, Stephen F., Thomas L. Madden, Alegandro A. Schäffer, Jinghui Zhang, Zheng Zhang, Webb Miller, and David J. Lipman $(1^{\log \alpha})_i$ "Gapped BLAST and PSI-BLAST: a new generation of protein database search RECEIVED

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Database: All non-redundant GenBank CDS translations+PDB+SwissProt+PIR+PRF

1,292,592 : equences; 412,925,052 total letters

Related Structures

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gi|6694394|gb|AAF25213.1|AF201833_1 FIL1 eta [Homo sapiens] 174 Le-42 171 1e-41 136 Ja-31 132 7e-30 gn: 20822718 | ref: XP | 130058.1 | RIKEN cDNA 2310043N20 [Mus mus... 1. = -2.4114 gi[25008591]sp[Q9D576 IIF8 MOUSE Interleukin I family membe... 110 6e-24 gi|6694392|gb|AAF25212.1|AF201832 1 FIL1 zeta [Homo sapiens] 70 3e-11 g1:19068184 | gb | AAL671:1.1 | IL-iF7d [Homo sapiens] 70 1.e-11 49 ai:10185738|ab(AAG14411.1(AF251119 1 interleukin-1-related ... •..e-11 gi|20127524|ref.NP 055254.2 interleukin 1 family, member 7... £.G ~'e-11 $gi | 6912452 | ref | NP = \overline{0}36407.1 |$ interleukin I family, member 5 ... 60 1.0-019 $\mathfrak{g}_1 \mid 20070252 \mid \text{ref NP} \mid 059253.2$ interleukin 1 family, member 9... £() 4-2-08 prodesessor sploagy Interleukin I family membe... 50, " = = (+9 g:[9506807]ref[NP_062024.1] interleukin 1 family, member 5 ...
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g1 208635 gb AAA72561.1 interleukin 1-beta	47	4e-04
g1 5777787 emb CAB53499.1 interleukin-1-beta [Xenopus laevis]	46	4e-04
g1 1708446 sp P51493 IL1B_MACNE INTERLEUKIN-1 BETA PRECURSO	46	4e-04
g1 1352451 sp P48090 IL1B MACMU INTERLEUKIN-1 BETA PRECURSO	46	4e-04
gi 3024024 sp P79182 IL1B MACFA INTERLEUKIN-1 BETA PRECURSO	46	4e-04
g1 3687837 gb AAC62237.1 interleukin-1 receptor antagonist	46	5e-04
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mail:0:0.05025 qk AAN76442.1 interleukin-1 beta precursor [Ma	40.	6e-04
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gr 494152 pdb 1HIB Interleukin-1 Beta (Human) Mutant With	46	6e-04
gi 1827779 pdb 1IOB Interleukin-1 Beta From Joint X-Ray A	46	7e-04
gi 230410 pdb 21BI Interleukin-1Beta (IL-1Beta) (Mutant W	46	7e-04
g1 230947 pdb 41BI Interleukin-1Beta (IL-1Beta) (Mutant W	46	7e-04
gi 230798 pdb 31BI Interleukin-1Beta (IL-1Beta) (Mutant W	46	7e-04
gi 2905622 gb AAC03536.1 interleukin 1 beta [Homo sapiens]	45	7e-04
g1 186288 qb AAA59136.1 interleukin 1	45	7e-04
g2 35 35 6 gb AAK91041.1 AF294754 1 interleukin-1 beta [Sa	45	9e-04
g1 0025027 gb AAN76445.1 interleukin-1 beta precursor [Pa	45	0.001
gi 208637 gb AAA72849.1 growth hormone:interleukin 1-beta	45	0.001
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g1 5"08097 emb CAB52366.1 interleukin-1-beta [Cyprinus car	43	0.004
g1 1170530 sp P46648 IL1B_CERTO INTERLEUKIN-1 BETA PRECURSO	43	0.006
gi 3211709 gb AAC39256.1 interleukin-1 beta [Equus caballus]	43	0.006
gi 124306 sp P14628 IL1B_RABIT INTERLEUKIN-1 BETA PRECURSOR	42	0.006
gi 16945693 emb CAD11603.1 interleukin-1 beta [Sparus aura	42	0.007
gi 25956.74 emb CAC33867.2 interleukin 1 beta protein [8co	4()	0.032
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gi 15489057 gb AAHI3644.1 Similar to replication initiatio	. 1	1.4
on'USI/739 [emb[CAD12102.1] interleukin-1 beta-1 [Carassius		3.0
,		



EXHIBIT B

IL-lra-L	10 20 30 40 50 ATGAGG STCACAAA GATCCAT SIGA GAAGGATGGCTTCCTGGGGTCACAC TAUTCICAGT STTTCTAGGTACCCTACCGAAGGACCCCAGT GTG
IL-lra-L	(.0 70 50 60 10) ATTCACTCAC DACTT DCTTT 39 CTG 3 3A3TG 3GGGCTCCCTT 3GTTA CAT TAAGTGAGT 3 3TGAA 3GAAA DD 3A DDDTCAC DCCCGAGGGAA CCAAT STA
IL-Ira-L	110 120 130 140 150) GTCACTCCAGGGTGSSTTGTTSCTCCCCCCTTTTCTTCATTCTCCATGG CAGTGAGGTCCCACCCAACAACGASSSGGGAAAAGAAGTAAGAGGTACC
IL-ira-L	180 170 180 190 200 GTTGTTTCCCTGATCAGTCCCAATGCGAGTACCTGGATATATCAGTTGAA CAACAAAGGGACTAGTCAGGGGTTACGCTCATGGACCTATATAGTCAACTT
IL-lra-L	21) 22) 230 240 250 GACTTTGAA GCCTGA GAAAACA GACTATGTTTATGTGAAGCTTTTGTTTC CTGAAACTTCGGACTCTTTTGTCTGATACAAATACACTTCGAAAACAAAG
TL-lra-L	260 270 280 290 300 TGGAGATGAAAATAG JAGAG JAAGA GGAATGATGAAAAAATTCACTGTT ACCTCTACTTTTATCGTCTCGGTTCTCCTTACTACTTTTTTAAGTGACAA
IL-1ra-L	310 320 330 340 350 GGACTATAT GGAAAA CICAG SCITGT STIPONT GGT CTTTGAGT GAACTATT CCTGATATA CCTTTTGAGTG C SACA CAAGTA CCAGAAACTCA CTTGATAA
Th-Ira-L	360 370 330 390 400 TT CAACATT GAAAATT GACACA DOT CA GUGG GGGAGCATT CAGGATAT CA AAGTT GTAA CTT GT GT GGAGT CGCC CCCT CGT AAGT CCT AT AGT
ii lee b	41 40 40 40 40 44 44 45 ATSATSOGGTGTGGTTGTTGAGAGGAGA 19GT ATAG AGG 15 SGAGG TAGTAGG GGAGAG MAGAAGIGGTGTGTGAGTAT STGAGGGG
!. GPOIL I • 4]	40 TATTCAATCAGGGTVA-ATVTGVAGATTGGV
Ilinaha L	THE THE THE THE THE THE THE

IL-ira-L	460 470 480 490 500 AAGGACCGTATGTCTCCAGTCACTATTGCCTTAATCTCATGCCGACATGT TTCCTGGCATACAGAGGTCAGTGATAAUGGAATTAGAGTACGGCTGTACA
1. SPOIL I [604] IL Tra-L	AA AA
IL-1ra-L	510 520 530 540 550 GGAGAC DOTT GA GAAA GACAGAGG GGACU DOATOTACOT GGGCOT GAATG DOTOT GGGAA DT DTTT DTGTOT DO DOT GG GGTAGATGGACOUGGA DTTA D
1. SPOIL I [604] IL ira-L	120 130 140 150 160 GCATCACCTTCGCTTAGACAT-STTCASGATCTTAGTAGTCGTGTG>
IL-ira-L	560 570 580 590 600 GACTCAATCTCTGCCTGATGTGTGCTAAAGTCGGGGACCAGCCCACACTG CTGAGTTAGAGACGGACTACACACGATTTCAGCCCCTGGTCGGGTGTGAC
1. SPOIL I [604] IL-Ira-L	DC
II-lra-L	610 620 630 640 650 (AGCTGAAGGAAAAGGATATAATG SATTT STACAA CCAACCUGAGCCTGT GTCGACTTCCTATATTACCTAAA CATGTT SGTTGGGCTCGGACA
i. SPOIL I [604] IL 114 L	U 220 230 240 250 CAGTTCCAGGAAGGGAACATAATG SAAAT STACAA CAAAAAGGAACCTGTO HII I IIIII I IIIIIII IIIIIIII IIIIIIII
II. Lea L	A A COMPANIAN AND A COMPANIAN
SPCIL I	DT - DBB DBB BBB BBB BBB BBB BBB BBB BBB B

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i. Mail i	320	3 3:1	3.4	÷ 4 - 5	
(Colin	AGTCTGCAGCCTTC	CCTGGTT 3GT	TCATCGCTGT	CTGCTCTAAA	GGGAGC ·
T.T. 1. T.					11 11
IL-lra-L	AGTOTGTGGCTTTO	JUTISISUT SGI	TCATUSCISI	United TOTOme	باحا فلإعمامات
	760	7.70	73.1	7611	800
11-114-1	T ST COTOT CATOC'I'				
	A JA GGAGAGTAGGA	ATGGGTT CI'I	'GACCCCTTTC	GGTTGTGATG	iacTGAA
:. SHOIL I	370	380	39.)	490	
[604]	TGCCCAUTCATTCT	GACCCAA GAA	CTGGGGGAAA	TCTTCATCAC	TGACTT:
IL-ira-L	TGTCCTCTCATCCT	TACCCAAGAA	TITITITITI .CTGGGGAAAG	IIIIII GCCAACACTAC	TGACTT
	810				
IL-lra-L	TGGGTTAACTATGC	rgttt			
	ACCCAATTGATACGA	ACAAA			
1. SPOIL I	0 420				
[604]	C SAGATGATTGTGG	Γ>			
:L-lra-L	 T GGGTTAACTATGC	 			
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EXHIBIT C

	<u></u>	20	3:	-1	5.0
IL-lra·L	AT GAGG ST CAC	AAA JATCCAT	GGGAGAA GCAT	GGCTTCCTGG	GTCACAC
	TACTICCIAGT	TTT CTAG STA	CCCT CTT CGTA	JODAE ĐAAE DU.	MASTOTE
		3.0			
T. T		70			
IL-lra-L	ATTCACTCACE TAAGTGAGTGG				
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	110	120	130	140	150
IL-lia-L	GTCA JTCCAGG	GTGGGTTGTT	GCT CACC CCCT	TTTCTTCATT	TCCATGG
	CAGTGAGGTCC	CACCCAACAA	CIGAIGIGIGIG GGGA	AAAGAAGTAA	JAGGTACC
TT 0. T		170			
IL-lra-L	-GTTGTTTCCCT -CAACAAAGGGA				
		COLMICTION COL	ITAUJUUT JAT J	SASSIAIAIN.	31 CAAO1 1
	210	220	230	240	250
IL-1ra-L	GACTTTGAAGO	CTGAGAAAAC	AGACTAT STTT	AT 3TGAAGCT1	TTGTTTC
	CTGAAACTTCG	GACTCTTTTG	FCTGATA CAAA	TA CACTTCGAA	AAACAAAG
1. IL-lra β					
[1002]					C>
IL-lra-L					C
10 110 1					
	260	270	230	290	300
IL-lra-L	TGGAGATGAAA	ATAGCAGAGC	CAAGAGGAAT G	AT BAAAAAAT	CACTSTT
	ACCTCTACTTT	TATCGTCTCG	GTTCTCCTTAC	TA CTTTTTAA	AGTGACAA
I. IL-ira β			50 300 3333 330 3		
[11772.]	TGTAGATAA				
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IL-1ra-L	37.0 37.0 39 39 39 39 4 99 TTCAACATTGAAAATTGACACCTCAGCGGGGGGGGAGCATTCAGGATATCA AAGTTGTAACTTTTAACTGTGTGGGAGTCCTATAGT
l. IL Ira β [1002]	130 140 150 150 150 150 150 150 150 150 150 15
IL-lra-L	TT DAACATTGAAAATTGA DACA DOT DAGO GG GG GA GCATTCA GGATAT DA
IL-1ra-L	410 420 430 444 450 AT DAT DESERT STEERTCAT DA SEA DOCT CATAGOA STUCCIGA SE TA STA SCOCA DA DICAAGAA STIDUT SGTUT SUGAGTAT COT DA GGGCT DI
1. IL-1ra β [1002]	
IL-lra-L	######################################
IL-Ira-L	460 470 480 490 500 AAGGACCGTATGTCTCAGTCAGTCAGTTAATCTCATGCCGACATGT TTCCTGGCATACAGAGGTCAGTGAGTAACGGAATTAGAGTACGGCTGTACA
	T
1. 1L-1ra β [1002]	220 230 240 250 260 AAGGACAGTGACCCCAGTCACTGTTGCTGTTATCACATGCAAGTATCC>
IL-1ra-L	AAGGACCGTATGTCTCCAGTCACTATTGCCTTAATCTCATGCCGACATGT
IL-ira-L	510 520 530 540 550 GGA-GACCCTTGAGAAAGACAGA GGGGACCCCATCTACCTGGGCCTGAATG CCTCTGGGAACTCTTCTGTCTCCCCTGGGGTAGATGGACCGGGACTTAC
	AAT
1. IL-1ra β [1002]	270 230 290 300 AGAGGCTCTTGAGCAAGGCAGAGGGGATCCCATTTATTTGGGCCAGAATC>
11 123 1	GRAGAC NOTTGARGAAARACAGAGA OO WAX TACCITOGG CIICAATG
ii .ra i	
I. Thelra B	26 330 340 850 600 UA-GRAATOTOTOTO ATHTOTOACACOTTOGACCACCACCACCACCACCACCACCACCACCACCACCACC

II. ligavi	C10 620 630 649 650 caget BAABGAAAAGBATATAATGGATTTGTACAACCAAACCAGAGCCTBT GTCBACTTTCCTATATTACCTAAACATGTTGBTTGGGCTCGGACA
1. IL-1ra β [1902]	370 390 390 400 41 CAG DTAAAAGAGCAGAA SATCATGGATCTGTATGGCCAACCCGAGCCCGTG
IL-lra-L	CAG DT GAA GGAAAAG GATATAAT GGATTT GTACAAD DAACD SAGCOT GT
IL ira-L	3 6k) 670 680 (80) 700 GAAST COTTTOTOTTOTACCACAGGCAGAGTGGCAG SAAUTCCACUTT IS CTT DA SAAAGAGAAGATGGTGTGTGGGT UTCACUGTC ITTGAGGTGGAA SI
1. IL-1ra β [1002]	420 430 440 450 460 GAAACCCTTCCTCTCCCGTGCCAAGACTGGTAGGACCTCCACCCTTG>
IL-lra-L	GAAGT CCTTTCTCTTCTACCACAGCCAGAGTGGCAGGAACTCCACCTTCC
IL-lra-L	710 720 730 740 750 AGTGT STG-SCTTTCCCT SGCTG-STTCATCGCTGTCAGCTCTGAAGGA S SC TCAGA CAG CGAAAAGGGA-CCGA-CCAAGTA-GCGA-CAGT CGAGA-CTTCCT C CG
1. IL-1ra β [1002] IL-1ra-L	470 480 490 500 510 AGTCT STGSCCTTCCCGSACTGGTTCATTGC+CTC+-CTCCAAGAGA SAC>
	760 77 0 780 790 300
IL-1ra-L	TGTCCTCTCATCCTTACCCAAGAACTGGGGAAAGCCAACACTACTGACTT ACAGGAGAGAGTAGTGACTCTTGACCCCTTTCGGTTGTGATGACTGAA
1. TL-1ra β [1002]	520 530 540 550 560 caggggat cattergagtecata saactig sgaagt catacaacagggtt>
IL-lra-L	TGTCCTCTCATCCTTACCCAAGAACTGGGGAAAAGCCAACACTACTGACTT
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IL lra-L	TOGGTTAACTAT



EXHIBIT D

IL-Ira-L	10 ATGASGSTCACAA TAUT COCAGTSTT			ROTTOOTIGGG	
IL-1ra-L	OB ATTCACT CACCAC TAAGTGA STGGTG	TTCCTTTGGC'	r sggagtggg	GCTCCCTTGC	TTACAT
Ib-lra-L	11) GTCACTCUAGGGT CAGTGAG FTCCCA	GGGTTGTTGC:		PTCTTCATTCT	CCATGG
TL-lra-L	100 GTTGTTTCCCTGA CAACAAAGGGACT.	TCAGTCCCAA		rggatatatov	\GTTGAA
IL-lra-L	21) GACTTTGAAGCCT CTGAAACTTCGGA	GAGAAAA CAGA		rgtgaagctti	TGTTTC
IL-ira-L	.260 TGGAGATGAAAAT. ACCTCTACTTTTA	AGCAGAG CCAA		rgaaaaaatir:	ACTGTT
i. IL-1ra [522] IL-1ra-L		:	20 ACA-GAATG 	! !	
TL-ira-L	310 GGACTATATGGAA CCTGATATACCTT	AACTCAG GCT(rCTTTGAGTGA	AACTATT
11 . 13 . 13 . 13	4 TO MATERIAL WATER	, A NOTO AATOMA			TIM :
11 12 4 1	GGA TATATAA	AACT GEGET			.f. 125111

	360 370 358 358 400
IL-limi-L	TT CAACATTGAAAATTGACACACCT CAGCGGGGGAGCATT CAGGATATCA AA STTGTAACTTTTAACTGT STGGAGT CGCCCCCTCGTAAGTCCTATA ST
	AAA
1. II. lia [544]	FO 100 110 120 130 TTC-ASAGAGGATCTGCCCACC-CTCTGGGAGAAAATCCAGGATGCAA
L-ira-L	TID ASA GACGATOTGGGGAGC GIGIGGGGGGGGGGGGGGGGGGGGGGGGGGGG
in int	. 1 SAMUAI, GAAAAI 1 GASA SAGASA GAGASA GAA IX A SAATAI SA
IL-Ira-L	410 420 430 440 450 AT CAT OG SGT GT G SGTTCTT CAGGACCAGA C SUT CATAGCAGT COUGA SG TAGTAGCCCACA CCCAAGAAGT CCT GGT UT G CGAGTAT CGT CAGGGCT CC
	A T
1. fL-1ra 522 1	140 150 160 170 GCCTTGGAATGTSGGATGTT-AACCAGAG-ACCT-TCTAT-CTGAGG>
TL-lia-L	
TL-1ra-L	460 470 430 490 500 AA SGACC STATGT CTCAGT CACTATT SCCTTAATCTCATGCCGACAT ST TTCCTGG CATACA SAGGTCA STGATAAC SGAATTAGAGTACGGCTGTA CA
	A
1. IL-1ra 1 522 1	
IL-lra-L	AACAACCAACTAGTTGCTG-GATACTTGCAATTTGAZTTTGAZTTTGAZTTTGAZTTTGAZTCTAATTTGAZTCTAATTTGAZTCTAATTTGCCGACATGTCAATTGCCGACATGTCAATTGCCGACATGTCAATCTCATGCCGACATGTCAATCTCATGCCGACATGTCAATCTCATGCCGACATGTCAATGTCAATCTCATGCCGACATGTCAATCTCATGCCGACATGTCAATCTCATGCCGACATGTCAATGTC
TT-TL%-T	AAGGACCGTATGTCTCCAGTCACTATTGCCTTAATCTCATGCCGACATGT
IL-Ira-L	510 520 530 540 550 GGA:GACCETTIGA:GAAAGACA GAGGGGACCCATCTACCTGGGCCTGAATG
	CCTCTGG 3AACTCTTTCTGTCTCCCCTGGGGTAGATGGACCCGGACTTAC
	T TGCTC
	ur i lar i l
11. 11.4 1.	RIAGA COTT SASAAA SACAGAGGGA COCCATOTA COD E COCT GAATG

11-11a-L	560 570 580 590 600 GACTCAATCTCTGCCTGATGTGCTAAAGTCGGGGGACCAGCCCACACTG CTGAGTTAGAGACGACTACAGACACGAGCCCGGTGGGTCCGGTGTGAC
	Т
1. IL lia [520]	290 330 310 310 55 GAGGGAAGATGTGCCTGTGTGTGAAGTCGCTGATGAGACCAGACTC> FI
TL-1:4-L	GAUT CAAT OT CTGCCTGAT ST ST SCTAAA ST CGGGGACCAGCCCA CACT S
IL-1ra·L	C10 62) 63) 640 65) CAG DT BAAGGAAAAGGATATAAT BEATTT BTACAACCAACCCGA BUCTET GTCBACTTCCTTTTCCTATATTA DCTAAACATGTTGGTTTGGGCTCGGA CA
1. IL-1ra [522]	340 350 360 370 380 caget sagegagaacagaagagaga
IL-ira-L	
IL-ira-L	660 670 680 690 700 GAAGT COTTTCTCTACCA DA SOCAGA STIGGCAGGAACTICCACCTTICG CTTICA SGAAAGAAGATGST STIDSGTCT DA DOGTCCTTGAGGTGGAA SC
1. IL-1ra [522]	390 400 410 420 430 CAA 9C 9CCTTCATCCGCT CAGACA 9T 9GCCCCACCACCACCACTTTT9>
IL-1ra-L	GAAGT COTTTOTTOTTOTACCA DA SOCAGA STEGCAGGAACT COACCTT DE
IL-1ra-L	710 720 730 74) 750 AGT CT STGGCTTCCCTGGCTGGTTCATC SCTGTCASCTCTGAAGGAGGC TCA SA CACUGAAAGGGACCGA DCAA STAG DGACAGTCGAGAUTT CCTCC S
	G
1. IL-1ra [522]	44) 450 460 170 480 AGTCTGCCGCCTGGTTGGTTCCTC TGCACAGCGATGAAGCTGAC>
TI-1ra-L	
	INTEGRATION ACTIONNY AREA CHARACTERRIA RAMAR REMARKA NA CHARTA A MARKA METARRIA MATERIATO CITURA E E ESTITO ERROTEST MATERA CITURA
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II. lia-L TGGGTTAACTATGCTGTTT ACCCAATTGATACGACAAA

i. IL-lia 540

AAATTCTACT-TCCAG -[ 522 ]

TGGGTTAACTATGCTG IL-1ra-L



### AMENDMENTS TO THE SPECIFICATION

### Marked Up Version of Replacement Paragraphs of Specification

### under 37 C.F.R. 1.121(b)(1)(iii)

Please amend the title at page 2, lines 1-2 to read as follows:

# NUCLEIC ACIDS ENCODING INTERLEUKIN-1 RECEPTOR ANTAGONIST-LIKE MOLECULES PROTEINS AND USES THEREOF

Please amend the paragraphs at page 3, line 16 to page 4, line 16 to read as follows:

The invention provides for an isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

- (a) the nucleotide sequence as set forth in SEQ ID NO: 1.
- (b) the nucleotide sequence of the DNA insert in ATCC Deposit No.
- (e)(b) a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 2;
- (d)(c) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of either (a) (c) or (b); and
  - (e)(d) a nucleotide sequence complementary to any of (a) (c).

The invention also provides for an isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

- (a) a nucleotide sequence encoding a polypeptide which is at least about 70 percent identical to the polypeptide as set forth in SEQ ID NO. 2, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO. 2;

- (d) a region of the nucleotide sequence of SEQ ID NO: 1, the DNA insert in ATCC Deposit No. ______, or any of (a) (c) comprising a fragment of at least about 16 nucleotides:
- (e) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a) (d); and
  - (f) a nucleotide sequence complementary to any of (a) (d).

Please amend the paragraphs at page 5, lines 12-29 to read as follows:

The present invention provides for an isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

- (a) the amino acid sequence as set forth in SEQ ID NO: 2; and
- (b) the amino acid sequence encoded by the DNA insert in ATCC Deposit No.

The invention also provides for an isolated polypeptide comprising the amino acid sequence selected from the group consisting of:

- (a) an amino acid sequence for an ortholog of SEQ ID NO: 2.
- (b) an amino acid sequence which is at least about 70 percent identical to the amino acid sequence of SEQ ID NO: 2, wherein the polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2;
- (c) a fragment of the amino acid sequence set forth in SEQ ID NO: 2 comprising at least about 25 amino acid residues, wherein the fragment has an activity of the polypeptide set forth in SEQ ID NO: 2, or is antigenic; and
  - (d) an amino acid sequence for an allelic variant or splice variant of the amino acid

Please amend the paragraph at page 8, line 29 to page 9, line 3 to read as follows:

The terms "IL-1ra-L gene" or "IL-1ra-L nucleic acid molecule" or "IL-1ra-L polynucleotide" refer to a nucleic acid molecule comprising or consisting of a nucleotide sequence as set forth in SEQ ID NO: 1, a nucleotide sequence encoding the polypeptide as set forth in SEQ ID NO: 2, a nucleotide sequence of the DNA insert in ATCC Deposit No. ______, and nucleic acid molecules as defined herein.

Please delete the paragraph at page 97, lines 26-29.



## AMENDMENTS TO THE CLAIMS

## Marked Up Versions of Amended Claims under 37 C.F.R. 1.121(c)(1)(ii)

1. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence
selected from the group consisting of:
(a) the nucleotide sequence as set forth in SEQ ID NO: 1;
(b) the nucleotide sequence of the DNA insert in ATCC Deposit No;
(c)(b) a nucleotide sequence encoding the a polypeptide as set forth in SEQ ID NO: 2;
(d)(c) a nucleotide sequence whichthat hybridizes under at least moderately or highly
stringent conditions to the complement of any of the nucleotide sequence of either (a) - (c) or (b):
and or
(e)(d) a nucleotide sequence complementary to the nucleotide sequence of any of (a) -
(c).
2. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence
selected from the group consisting of:
(a) a nucleotide sequence encoding a polypeptide which is at least about 70 percent
identical to the polypeptide as set forth in SEQ ID NO: 2, wherein the encoded polypeptide has an
activity of the polypeptide set forth in SEQ ID NO: 2;
(b) a nucleotide sequence encoding an allelic variant or splice variant of the nucleotide
sequence as set forth in SEQ ID NO: 1, the nucleotide sequence of the DNA insert in ATCC
Deposit No, or (a);
(c)(a)—a region of the nucleotide sequence of SEQ ID NO: 1, the DNA insert in ATCC
Deposit No ———————————————————————————————————
acid residues. wherein the polypeptide fragment has an activity of the encoded polypeptide as set
forth in SEQ ID NO: 2, or is antigenic.
(d)(b) a region of the nucleotide sequence of SEQ ID NO: 1, the DNA insert in ATCC
Deposit-No or-any-of (a) - (c) comprising a fragment of at least about 16

and or (f)(d) a nucleotide sequence complementary to the nucleotide sequence of any of (a) -(d)(c). 3. (Amended) An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of: a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at (a) least one conservative amino acid substitution, wherein the encoded polypeptide has an activity of is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 2: (b) — a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one amino acid insertion, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ ID NO: 2: (c)—a nucleotide sequence encoding a polypeptide as set forth in SEQ 1D NO: 2 with at least one amino acid deletion, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEO ID NO. 2; (d)(b) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2-which hasving a C- and/or N- terminal truncation, wherein the encoded polypeptide has an activity of the polypeptide set forth in SEQ 1D NO: 2 comprises at least 25 amino acid residues; (e)(c) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 2 with at least one modification-selected from the group consisting of that is a conservative amino acid substitutions, amino acid insertions, amino acid deletions. C-terminal truncation, and or Nterminal truncation, wherein the encoded polypeptide-has an activity of is at least 70 percent identical to the polypeptide set forth in SEQ ID NO: 2 and comprises at least 25 amino acid residues: (f)(d) a region of the nucleotide sequence of any of (a) -  $\frac{(e)}{(c)}$  comprising a fragment of at least about 16 nucleotides; the ride of a control of both relativities and have the real for the both of bights McDonnell Rochnen Hulbert & Berghoff 300 South Warker Drive Chicago, Illinois 60606 312 913.0001

(e)(c) a nucleotide sequence which that hybridizes under at least moderately or highly

stringent conditions to the complement of any of the nucleotide sequence of either (a) - (d) or (b).

(h)(f) a nucleotide sequence complementary to the nucleotide sequence of any of (a) - (e).

The process of Claim 8, wherein the nucleic acid molecule comprises promoter DNA other than the promoter DNA for the native IL-Tra-L-polypeptide promoter DNA operatively linked to the DNA a nucleic acid molecule encoding the an IL-Tra-L polypeptide.

The isolated nucleic acid molecule according to Claim 2, wherein the percent identity is determined using a computer program-selected from the group consisting of that is GAP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and or the Smith-Waterman algorithm.

45. (Amended) A <u>nucleic acid molecule encoding a fusion polypeptide comprising</u> the <u>polypeptide nucleic acid molecule</u> of any of Claims-13, 14, or 15 1, 2, or 3 fused to <u>DNA</u> encoding a heterologous amino acid sequence.

46. (Amended) The <u>fusion polypeptide nucleic acid molecule</u> of Claim 45, wherein the <u>DNA encoding the</u> heterologous amino acid sequence is <u>encodes</u> an IgG constant domain or <u>biologically active</u> fragment thereof.

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